

CLAIMS

What is claimed is:

1. A method for identifying a genetic locus that modulates a phenotype, the method comprising:
 - 5 (a) providing a renewable population of genetically diverse individuals; and
 - (b) mapping the genomes of individuals within the renewable population of genetically diverse individuals that display the phenotype, whereby a genetic locus that modulates the
10 phenotype is identified.
2. The method of claim 1, wherein the renewable population of genetically diverse individuals comprises:
 - (a) individuals produced by intercrossing recombinant inbred
lines;
 - 15 (b) individuals produced by backcrossing recombinant inbred lines;
 - (c) a cloned population of genetically diverse individuals; or
 - (d) a panel of cell lines derived from genetically diverse individuals.
- 20 3. The method of claim 1, wherein an individual of the renewable population of genetically diverse individuals comprises a diploid, tetraploid, or polyploid organism, or a cell derived there from.
4. The method of claim 3, wherein the organism is selected from a group consisting of an animal and a plant.
- 25 5. The method of claim 4, wherein the animal is a mammal.
6. The method of claim 5, wherein the mammal is a rodent.
7. The method of claim 6, wherein the rodent is a mouse.
8. The method of claim 2, wherein the recombinant inbred lines comprise less than about 500 lines.
- 30 9. The method of claim 8, wherein the recombinant inbred lines comprise less than about 100 lines.
10. The method of claim 2, wherein the recombinant inbred lines

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11. The method of claim 2, wherein the recombinant inbred lines
comprise recombinant inbred lines derived from at least 3 non-recombinant
5 parent lines.

13. The method of claim 12, wherein the recombinant inbred lines
10 comprise recombinant inbred lines derived from at least 8 non-recombinant
parent lines.

15. The method of claim 2, wherein the cloned population or the panel of cell lines is derived from recombinant inbred line intercrosses, recombinant inbred line backcrosses, an F2 population, or a natural population.

17. The method of claim 16, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 4 non-recombinant parent lines.

19. The method of claim 1, wherein the mapping comprises analysis
of genetic polymorphisms segregating in the renewable population of
30 genetically diverse individuals.

20. The method of claim 1, wherein the phenotype is selected from the group consisting of a visible phenotype, a physiological phenotype, a

behavioral phenotype, a susceptibility phenotype, a cellular phenotype, a molecular phenotype, and combinations thereof.

21. The method of claim 20, wherein the molecular phenotype is selected from the group consisting of a level of gene expression, a splice
5 selection, a level of protein, a protein type, a protein modification, a level of lipid, a lipid type, a lipid modification, a level of carbohydrate, a carbohydrate type, a carbohydrate modification, and combinations thereof.

22. The method of claim 1, wherein the phenotype is modulated by a non-genetic factor.

10 23. The method of claim 22, wherein the phenotype is modulated by an interaction between two or more non-genetic factors.

24. The method of claim 22, wherein the non-genetic factor is an environmental condition or drug exposure.

25. The method of claim 1, wherein the phenotype is modulated by an
15 interaction between a genetic locus and a non-genetic factor.

26. The method of claim 25, wherein the non-genetic factor is an environmental condition or drug exposure.

27. The method of claim 1, further comprising identifying two or more genetic loci that modulate the phenotype.

20 28. A method for producing a renewable population of genetically diverse individuals, the method comprising:

- (a) intercrossing recombinant inbred lines;
- (b) backcrossing recombinant inbred lines;
- (c) cloning a population of genetically diverse individuals; or
- 25 (d) generating a panel of cell lines derived from genetically diverse individuals.

29. The method of claim 28, wherein an individual of the renewable population of genetically diverse individuals comprises a diploid, tetraploid, or polyploid organism, or a cell derived there from.

30 30. The method of claim 29, wherein the organism is selected from a group consisting of an animal and a plant.

31. The method of claim 30, wherein the animal is a mammal.

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32. The method of claim 31, wherein the mammal is a rodent.
33. The method of claim 32, wherein the rodent is a mouse.
34. The method of claim 28, wherein the recombinant inbred lines comprise less than about 500 lines.
- 5 35. The method of claim 34, wherein the recombinant inbred lines comprise less than about 100 lines.
36. The method of claim 28, wherein the recombinant inbred lines comprise one or more recombinant inbred lines selected from the group consisting of mouse lines AXB, BXA, CXB, and BXD.
- 10 37. The method of claim 28, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 3 non-recombinant parent lines.
38. The method of claim 37, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 4 non-recombinant parent lines.
- 15 39. The method of claim 38, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 8 non-recombinant parent lines.
40. The method of claim 37, wherein the at least three non-recombinant parent lines comprise one or more non-recombinant parent lines selected from the group consisting of mouse lines C57BL/6, BALB/c, C3H, A, 129, and DBA/2.
- 20 41. The method of claim 28, wherein the cloned population or the panel of cell lines is derived from recombinant inbred line intercrosses, recombinant inbred line backcrosses, an F2 population, or a natural population.
- 25 42. The method of claim 41, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 3 non-recombinant parent lines.
43. The method of claim 42, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 4 non-recombinant parent lines.
- 30 44. The method of claim 43, wherein the recombinant inbred lines

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comprise recombinant inbred lines derived from at least 8 non-recombinant parent lines.

45. A renewable population of genetically diverse individuals produced by the method of claim 28.

5 46. A method for identifying an interaction between a genetic locus and a non-genetic factor, wherein the interaction modulates a phenotype, the method comprising:

- (a) providing a renewable population of genetically diverse individuals;
- 10 (b) providing a non-genetic factor to the renewable population; and
- (c) mapping the genomes of individuals that display the phenotype, whereby an interaction between a genetic locus and the non-genetic factor that modulates a phenotype is identified.

15 47. The method of claim 46, wherein the renewable population of genetically diverse individuals comprises:

- (a) individuals produced by intercrossing recombinant inbred lines;
- 20 (b) individuals produced by backcrossing recombinant inbred lines;
- (c) a cloned population of genetically diverse individuals; or
- (d) a panel of cell lines derived from genetically diverse individuals.

25 48. The method of claim 46, wherein the phenotype is selected from the group consisting of a visible phenotype, a physiological phenotype, a behavioral phenotype, a susceptibility phenotype, a cellular phenotype, a molecular phenotype, and combinations thereof.

30 49. The method of claim 48, wherein the molecular phenotype is selected from the group consisting of a level of gene expression, a splice selection, a level of protein, a protein type, a protein modification, a level of lipid, a lipid type, a lipid modification, a level of carbohydrate, a carbohydrate

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type, a carbohydrate modification, and combinations thereof.

50. The method of claim 46, further comprising identifying an interaction among two or more genetic loci and a non-genetic factor.

51. The method of claim 46, further comprising identifying an
5 interaction among a genetic locus and two or more non-genetic factors.

52. The method of claim 46, wherein the non-genetic factor is an environmental condition or drug exposure.

53. The method of claim 46, further comprising identifying an
10 interaction among two or more genetic loci and two or more non-genetic factors.

54. A method for identifying an epistatic interaction between genetic loci that modulate a phenotype, the method comprising:

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- 15 (a) providing a first renewable population of genetically diverse individuals;
 - (b) identifying individuals of the first renewable population that display a phenotype;
 - (c) mapping the genomes of the individuals of (b), whereby a first genetic locus that modulates the phenotype is identified;
 - 20 (d) establishing a second renewable population of genetically diverse individuals wherein the first genetic locus identified in (c) is held constant;
 - (e) identifying individuals among the second renewable population of genetically diverse individuals that display the phenotype; and
 - 25 (f) mapping the genomes of the individuals of (e), whereby a second genetic locus that epistatically interacts with the first genetic locus to modulate the phenotype is identified.

55. The method of claim 54, further comprising identifying an epistatic
30 interaction between gene networks.

56. A method for producing recombinant inbred lines, comprising:

- (a) intercrossing at least three non-recombinant inbred parent

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58. The method of claim 57, wherein the recombinant inbred lines comprise recombinant inbred lines derived from at least 8 non-recombinant parent lines.

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